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| EXAMINER | |
|---|---|
| LOCKARD, JON MCCLELLAND | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/868,967 | WALLUKAT ET AL. | |
| | Examiner | Art Unit | |
| | Elizabeth C. Kemmerer, Ph.D. | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 12-31* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 12-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-29 and 31* is/are rejected.

7)☒ Claim(s) *30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Application, Amendments, And/Or Claims*

The amendment of 05 June 2009 has been entered in full. Claims 6-11 are canceled. Claims 1-5 and 12-19 remain withdrawn from consideration as being directed to a non-elected invention. Claims 20 and 21 have been amended. Claims 27-31 have been added. Claims 20-31 are under examination.

### *Withdrawn Objections And/Or Rejections*

The objection to the disclosure regarding the title as set forth at p. 3 of the previous Office action (mailed 03 February 2009) is *withdrawn* in view of the amended title (received 05 June 2009).

The objection to the abstract as set forth at p. 3 of the previous Office action (mailed 03 February 2009) is *withdrawn* in view of the amended abstract (received 05 June 2009).

The objection to claim 20 for informalities as set forth at p. 3 of the previous Office action (mailed 03 February 2009) is *withdrawn* in view of the amended claim (received 05 June 2009).

### *35 U.S.C. § 112, Second Paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis of this rejection is set forth at item 12 of the previous Office action (mailed 03 February 2009). The issue set forth at item 11 has been resolved by the amendments to the claims (received 05 June 2009).

Applicant argues (p. 8, remarks received 05 June 2009) that claim 20 has been amended to clarify what additional method steps are required. This has been fully considered but is not found to be persuasive because the additional phrase only indicates what the significance of the binding is. It does not indicate, for example, if the binding occurs spontaneously after the contacting of the peptides to the body fluid, or if additional steps are required. Amending claim 20 to indicate that the contacting step is performed under conditions permitting binding of the autoantibodies to the peptides (similar to the wording provided in new claim 27) is one way of obviating the instant rejection.

***35 U.S.C. § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-29 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for (1) detecting autoantibodies against the angiotensin $AT_1$ receptor in a body fluid comprising contacting an isolated

peptide of the $AT_1$ receptor with a body fluid under conditions permitting binding of said autoantibodies with said peptide, wherein the peptide consists essentially of the amino acid sequence of SEQ ID NO: 1, and wherein the body fluid is maternal blood; or (2) binding autoantibodies against the angiotensin $AT_1$ receptor in a body fluid *in vitro*, comprising contacting an isolated peptide of the $AT_1$ receptor with a body fluid under conditions permitting binding of said autoantibodies with said peptide, wherein the peptide consists essentially of the amino acid sequence of SEQ ID NO: 1, and wherein the body fluid is maternal blood, does not reasonably provide enablement for the method as claimed, including achieving therapeutic or diagnostic results. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The basis of this rejection is set forth at pp. 4-10 of the previous Office action (mailed 03 February 2009).

Applicant's arguments (pp. 8-13, remarks received 05 June 2009) have been fully considered but are not found to be persuasive for the following reasons.

Applicant argues that Figure 2 shows the effects of a number of peptide sequences on the $AT_1$ receptor, and that only SEQ ID NO: 1 had inhibitor activity. Applicant points to Example 3 as describing a bioassay to detect antibodies. Applicant urges that Example 3 identifies ENTNIT (SEQ ID NO: 5), AFHYESQ (SEQ ID NO: 1), SHFYQTR (SEQ ID NO: 3), and GYYFDTN (SEQ ID NO: 4) as appropriate peptides. This has been fully considered but is not found to be persuasive. Even these four peptides are not representative of the scope of the generic claim (claim 20) which

recites a peptide of an $AT_1$ receptor comprising 5 to 30 amino acids of loop II of the receptor or functional analogs thereof. Furthermore, Figure 2 clearly shows that ENTNIT and three other peptides were ineffective.

Applicant argues that the amendments to claim 20 address the rejection's concern about structure predicting function. Applicant refers to Schneider et al. (of record) as evidence that the skilled artisan would have known how to screen for functional analogs. This has been fully considered but is not found to be persuasive. Claim 20 recites "or functional analogs thereof" which is broadly and reasonably interpreted as reading on any peptide of any structure that shares at least one function with the genus of peptides of an $AT_1$ receptor comprising 5 to 30 amino acids of loop II of the receptor. The instant fact pattern is similar to that in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), wherein a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a).

Applicant argues that the skilled artisan knew that individual amino acids sharing analogous physicochemical properties could be substituted for one another. This has

been fully considered but is not found to be persuasive. Again, the scope of the claims is far beyond a single, conservative substitution mentioned in the argument.

Thus, due to the large quantity of experimentation necessary to generate the infinite number of variants and derivatives recited in the claims and possibly screen the same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite meaningful structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicant argues that if binding of a peptide to an antibody is established, the skilled artisan knows how to accomplish this both *in vitro* and *in vivo*. Applicant urges that the peptides could be brought to the bloodstream of a patient for binding. Applicant argues that such would be useful diagnostically and therapeutically. Applicant argues that a proper correlation between *in vitro* and *in vivo* has been established. Finally, Applicant argues that p. 8 of the specification establishes that ENTNIT and AFHYESQ annulled the effect of autoantibody in hypertension sufferers, going beyond the scope of maternal blood. This has been fully considered but is not found to be persuasive. Page 7 shows that the peptide consisting of SEQ ID NO: 1 is able to bind and inhibit the effects of autoantibodies against the angiotensin $AT_1$ receptor, obtained from the gamma-globulin fraction of the serum of preeclampsia patients and in a culture

comprising cardiomyocytes. Contrary to Applicant's arguments, the specification fails to provide guidance regarding how to bind the autoantibodies *in vivo*. The skilled artisan would not know, without resorting to undue experimentation, that the administration of an undetermined amount of the peptide of SEQ ID NO: 1 would be able to bind the autoantibodies of the $AT_1$ receptor *in vivo*. In the previous Office action, Pettit et al. was cited as clear evidence in support of this position. Furthermore, *In re Colianni* was cited in the previous Office action as a court decision in agreement with the instant determination.

Claims 20-29 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis of this rejection is set forth at pp. 10-13 of the previous Office action (mailed 03 February 2009).

Applicant's arguments (pp. 13-15, remarks received 05 June 2009) have been fully considered but are not found to be persuasive.

Applicant argues that the amendments to the first independent claim limit the sequences to 5 to 30 amino acids of loop II of the $AT_1$ receptor. Applicant urges that such is supported considering the factors of level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics, and disclosure of methods of making. This is not found to be persuasive because claim 20

still recites "or functional analogs thereof." These can be of any structure. Therefore, Applicant's arguments do not reflect what is currently broadly claimed.

***Claim Objections***

Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ECK/
31 August 2009

/Elizabeth C. Kemmerer/
Elizabeth C. Kemmerer, Ph.D.
Primary Examiner, Art Unit 1646